UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/519,998	03/06/00	WILBUR D	33700W003

HM12/0723

SMITH GAMBRELL & RUSSELL LLP
1850 M STREET NW
SUITE 800
WASHINGTON DC 20036

EXAMINER	
WELLS, L	
ART UNIT	**PAPER NUMBER**
1619	9

DATE MAILED: 07/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/519,998	WILBUR ET AL.	
	Examiner	Art Unit	
	Lauren Q Wells	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26 and 28-30* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6,7* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Specification

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are: see 112 2nd rejections below.

Claim 27 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-10, 14-15, 17-19, 21-23, 30 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The phrase "derivatives, mutants or fragments" in claims 4 and 30 (lines 5-6), is vague and indefinite, as it is unclear what other compounds this term encompasses.

(ii) The phrase "essentially the same binding function" in claims 4, 5, 6, and 30 is vague and indefinite, as it is not clear how the binding function is similar or dissimilar.

(iii) The term "derivative" in claim 5, 7, 14, and 30 is vague and indefinite, as it is not clear what other compounds this term encompasses.

(iv) The term "preferably by bioinidase" in claims 7 and 10 (line 2-3) is vague and indefinite, as it is not clear if bioinidase is being claimed, if bioinidase is being solely claimed, or if there are other enzymes that break this bond.

(v) A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 7 (lines 4-5) recites the broad recitation "biotin derivatives", and the claim also recites "norbiotin or homobiotin" which is the narrower statement of the range/limitation.

In the present instance, claims 9, 18, and 22 (lines 2-4) recite a) the broad recitations "hydrogen bonding atoms", and the claims also recite "ethers or thioethers" which is the narrower statement of the range/limitation; b) the broad recitations "ionizable groups", and the claims also recite "carboxylates, sulfonates, or ammonium groups" which is the narrower statement of the range/limitation.

In the present instance, claim 14 (lines 4-7) recites a) the broad recitation "amino-carboxy derivatives", and the claim also recites "EDTA and DTPA derivatives, including Me-DTPA, CITC-DTPA, and cyclohexyl-DTPA. . ." which is the narrower statement of the range/limitation; b) the broad recitation "cyclic amines", and the claim also recites "NOTA, DOTA, and TETA for In. . .radionuclides" which is the narrower statement of the range/limitation.

In the present instance, claim 15 (lines 2-7) recites a) the broad recitation "positron imaging radionuclides", and the claim also recites "Fi18, Br-75, Br-76, and I-124" which is the narrower statement of the range/limitation; b) the broad recitation "therapeutic radionuclides", and the claim also recites "Y-90. . .Ra-223" which is the narrower statement of the range/limitation; c) the broad recitation "gamma imaging radionuclides" and the claim also recites "Tc-99m, In-111 and I-123" which is the narrower statement of the range/limitation. In the present instance, claims 17 and 21 (lines 2-3) recite the broad recitation "length of 1-25 atoms", and the claims also recite "length of 6-18 atoms, or groups of atoms" which is the narrower statement of the range/limitation.

In the present instance, claim 19 (lines 3-5) recites the broad recitation "active esters", and the claim also recites "N-hydroxy succinimide esters, sulfo-n-hydroxysuccinimide esters, phenolic esters" which is the narrower statement of the range/limitation.

(vi) The phrase "any other biotin binding species" in claim 8 (lines 4-5) is vague and indefinite, as it is not clear what other species, compounds, conjugates, or something else, are encompassed by this phrase.

(vii) The term "diminished" in claim 8, the term "active" in claim 19 (line 3), and the term "low" in claim 28 (line 15) are relative terms which render the claims indefinite. The terms

"diminished", "active", "low" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(viii) Claims 14, 15, 19, 23 are rejected for the use of improper Markush groups. See MPEP 2173.05(h) for examples of proper conventional or alternative Markush-type language (e.g., ". . .selected from the group consisting of. . .and . . .").

(ix) Claim 19 is rejected as vague and indefinite, as it is not clear where the listing of "active esters" ends. Are the aryl or alkylhydrazines "active esters"?

(x) Claim 19 provides for the use of the reagent of claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim19 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

(xi) The term "means" in claim 28 (lines 10 and 14) is vague and indefinite, as it is not clear what this term is referring to. The specification does not define the term and one of ordinary skill in the art would not be appraised of it.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilbur et al. (WO 97/29114).

Wilbur et al. teach biotin-containing compounds and biotinylation reagents incorporating soluble linker moieties. Biotin compounds disclosed include biotin, desthiobiotin, biotin sulfone, and iminobiotin. Homotrifunctional or heterotrifunctional linkers are disclosed, wherein these linkers may be coupled to a functional moiety and a biotin moiety and a third coupling site on the linker, wherein the third site may be radiolabeled and fluorescent molecules, proteins, peptides, antibiodies, and conjugating molecules. Positron emitting radionuclides disclosed for use include F-18, Br-75, B4-76, and I-124. Water solubilizing biotin-chelate conjugates are disclosed, wherein EDTA, DTPA, NOTA, DOTA, and TETA are disclosed as chelates, and wherein the chelates may be attached to radionuclides. Streptavidin is disclosed as being cross-linked with biotin derivatives. Applications of these compounds include as targeting agents, diagnostic agents, or therapeutic agents. Disclosed (compound 56) is a trifunctional biotin-containing reagent comprising biotin, a conjugation group (maleimide) and a radiohalogenated moiety. See Pg. 1, line 26-Pg. 7, line 2; Pg. 8, line 12-pg. 40, line 17.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-26 and 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilbur et al. in view of Yau et al. (5,541,287) or Theodore et al. (5,578,287) and Maddock (5,474,772).

Wilbur et al. fail to teach a method of diagnosing or treating and kits (see above disclosure).

Yau et al. teaches pretargeting methods and compounds. Certain embodiments of the compounds include chelate-biotin compounds and conjugates incorporating a chelate and a chemically modified biotin compound useful in diagnostic or therapeutic pretargeting methods. Disclosed is a method of diagnosis/treatment wherein an antibody-ligand conjugate is administered followed by an anti-ligand compound that binds unbound antibody-ligand conjugate from the blood. Further disclosed is a kit. See Col. 1, line 42-Col. 2, line 50; Col. 4, line 49-Col. 7, line 3; Col. 95, line 22-line 35.

Theodore et al. teach three-step pretargeting methods using improved biotin-active agents. Preferred biotin-active agents include Y-90-DOTA-biotin conjugates. A method of

diagnosis/treatment is disclosed wherein the antibody-ligand conjugate is administered followed by anti-ligand compound that clears unbound antibody-ligand conjugate from the blood. Further disclosed is a kit. See abstract; Col. 4, line 11-Col. 6, line 33; Col. 61, line 36-line 25.

Maddock teaches a method of therapeutic or diagnostic treatment comprising administering a medical agent and thereafter extracorporeally removing agent by passing bodily fluid over a support adapted to immobilize agent. See col. 1, line 15-Col. 2, line 1; Col. 4, line 65-Col. 6, line 2.Col. 9, line 29-Col. 10, line 46.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the teachings of Yau et al. or Theodore et al. into the invention of Wilbur et al. and obtain a method for diagnosis or treatment of a mammalian condition or disease and obtain a kit because a) Wilbur et al., Yau et al., and Theodore et al. all teach biotin conjugates as active agents for diagnostic and therapeutic use; b) Wilbur et al., Yau et al., and Theodore et al. all teach biotin as radiolabeled; c) Wilbur et al., Yau et al., and Theodore et al. all teach antibodies as targeting moieties. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of the combined references using the teachings of Maddock and obtain a method for diagnosis or treatment of a mammalian condition or disease comprising extracorporeally eliminating non-tissue-bound therapeutic or diagnostic biomolecule conjugates because a) Maddock teaches that his invention may be applied to nearly any treatment procedure with a medical agent that would benefit by artificial clearance, such as a cancer treating/diagnostic agent that is harmful when lingering in the body ; b) the combined references teach radiolabled biotin for use in treating cancer therapeutically and diagnostically.

The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Prior Art

The prior art made of record and not specifically relied upon in any rejections cited above is either 1) considered cumulative to the prior art that was cited in a rejection or is 2) considered pertinent to the applicant's disclosure and shows the state of the art in its field but is not determined by the Examiner to read upon the invention currently being prosecuted in this application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana L Dudash can be reached on (703) 308-2328. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
June 11, 2001

DAMERON L. JONES
PRIMARY EXAMINER